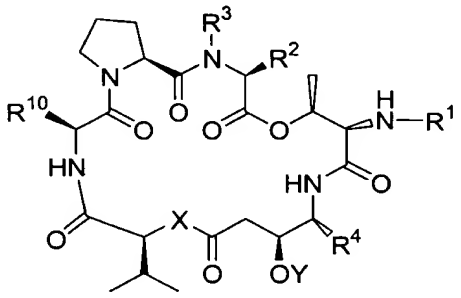
Amendments to the Claims

Please add new claim 62.

The listing of claims will replace all prior versions and listings of claims in the application.

1. (Currently Amended) A ~~composition comprising a~~ tamandarin compound ~~analog~~ having the structure



wherein:

i) R^1 is selected from the group consisting of

-(N-methyl)leucine-deoxo-proline,

-(N-methyl)leucine-deoxo-proline-lactate,

-(N-methyl)leucine-deoxo-proline-pyruvate,

-(N-methyl)leucine-deoxo-proline-lactate-(a first fluorophore),

-(N-methyl)leucine-deoxo-proline-lactate-glutamine-pyroglutamate,

-(N-methyl)leucine-deoxo-proline-lactate-glutamine-cyclopentanoate,

-(N-methyl)leucine-deoxo-proline-alanine-leucine-pyroglutamate

-(N-methyl)leucine-deoxo-proline-(N-methyl-alanine)-leucine-pyroglutamate,

-(N-methyl)leucine-dehydro-proline,

-(N-methyl)leucine-dehydro-proline-lactate,

-(N-methyl)leucine-dehydro-proline-pyruvate,

-(N-methyl)leucine-dehydro-proline-lactate-(a first fluorophore),

-(N-methyl)leucine-dehydro-proline-lactate-glutamine-pyroglutamate,

-(N-methyl)leucine-dehydro-proline-lactate-glutamine-cyclopentanoate,

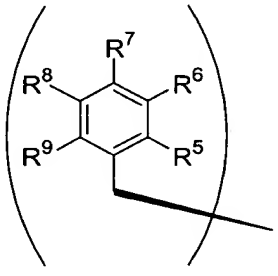
-(N-methyl)leucine-dehydro-proline-alanine-leucine-pyroglutamate, and

-(N-methyl)leucine-dehydro-proline-(N-methyl-alanine)-leucine-pyroglutamate;

ii) R^2 and R^3 are one of

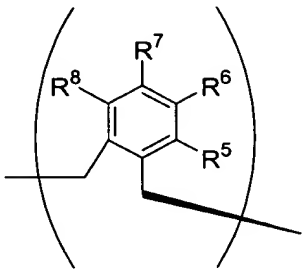
(a) R^3 is selected from the group consisting of $-CH_3$ and -H;

and R^2 is selected from the group consisting of an isoleucine side chain, a valine side chain, an alanine side chain, a norleucine side chain, a norvaline side chain, a leucine side chain, a histidine side chain, a tryptophan side chain, an arginine side chain, a lysine side chain, a second fluorophore, and a substituent having the structure



; and

(b) R^2 and R^3 together are a substituent having the structure



iii) each of R^5, R^6, R^7, R^8, and R^9, when present, is independently selected from the group consisting of -H, -OH, $-OCH_3$, $-CO(C_6H_5)$, -Br, -I, -F, -Cl, $-CH_3$, and $-C_2H_5$;

iv) R^4 is selected from the group consisting of an isoleucine side chain and a valine side chain;

v) X is selected from the group consisting of -O- and -NH-;

vi) Y is selected from the group consisting of -H and a hydroxyl protecting group; and

vii) R^{10} is selected from the group consisting of a leucine side chain and a lysine side chain [[; and

viii) the molecule is not tamandarin A]].

2. (Currently Amended) The ~~composition~~ compound of claim 1, wherein R^1 is selected from the group consisting of

-(N-methyl)leucine-deoxo-(S)proline,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate,

-(N-methyl)leucine-deoxo-(S)proline-pyruvate,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(a first fluorophore),

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-glutamine-pyroglutamate,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-glutamine-cyclopentanoate,

-(N-methyl)leucine-deoxo-(S)proline-alanine-leucine-pyroglutamate,

-(N-methyl)leucine-deoxo-(S)proline-(N-methyl-alanine)-leucine-pyroglutamate,

-(N-methyl)leucine-dehydro-(S)proline,

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate,

-(N-methyl)leucine-dehydro-(S)proline-pyruvate,

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate-(a first fluorophore),

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate-glutamine-pyroglutamate,

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate-glutamine-cyclopentanoate,

-(N-methyl)leucine-dehydro-(S)proline-alanine-leucine-pyroglutamate and

-(N-methyl)leucine-dehydro-(S)proline-(N-methyl-alanine)-leucine-pyroglutamate.

3. (Currently Amended) The ~~composition~~ compound of claim 1, wherein R^1 is selected from the group consisting of

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(S)glutamine-(S)pyroglutamate,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(S)glutamine-(S)cyclopentanoate,

-(N-methyl)leucine-deoxo-(S)proline-(S)alanine-(S)leucine-(S)pyroglutamate, and

-(N-methyl)leucine-deoxo-(S)proline-(N-methyl-S-alanine)-(S)leucine-(S)pyroglutamate,

-(N-methyl)leucine-deoxo-(S)proline-pyruvate,

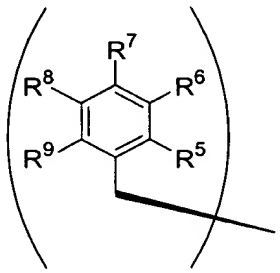
-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(a first fluorophore),

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(S)glutamine-(S)pyroglutamate,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(S)glutamine-(S)cyclopentanoate,

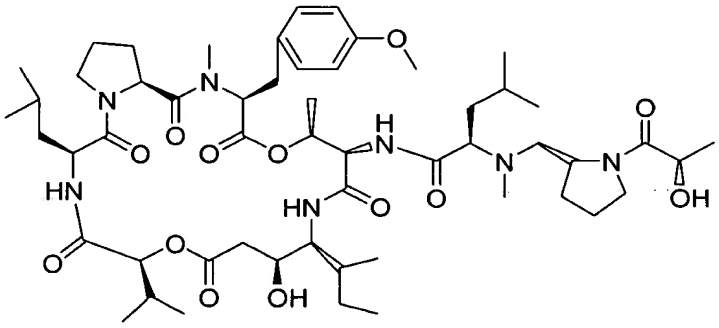
-(N-methyl)leucine-deoxo-(S)proline-(S)alanine-(S)leucine-(S)pyroglutamate, and -(N-methyl)leucine-deoxo-(S)proline-(N-methyl-S-alanine)-(S)leucine-(S)pyroglutamate.

4. (Currently Amended) The ~~composition~~ compound of claim 1, wherein R^2 is

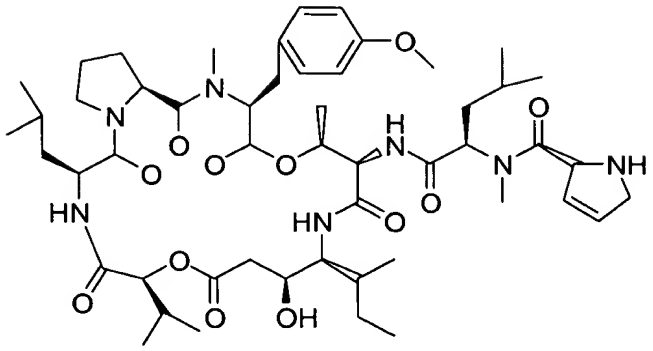


R^3 is methyl, R^4 is an isoleucine side chain, each of R^5, R^6, R^8, and R^9 is -H, R^7 is methoxy, R^{10} is a leucine side chain, X is -O-, and Y is -H.

5. (Currently Amended) The ~~composition~~ compound of claim 1, wherein the tamandarin ~~analog~~ is compound 201 having the structure

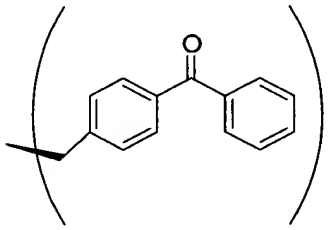


6. (Currently Amended) The ~~composition~~ compound of claim 1, wherein the tamandarin ~~analog~~ is compound 203 having the structure



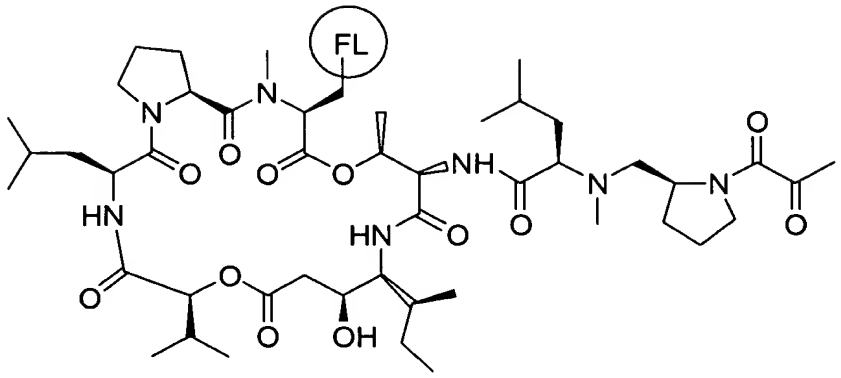
7. (Currently Amended) The ~~composition~~ compound of claim 1, wherein R^1 is -(N-methyl)leucine-deoxo-(S)proline-lactate.

8. (Currently Amended) The ~~composition~~ compound of claim 1, wherein Y is -H, and wherein R^2 has the structure



9. (Currently Amended) The ~~composition~~ compound of claim 1, wherein R^2 is a lysine side chain and Y is -H.

10. (Currently Amended) The ~~composition~~ compound of claim 1, wherein the ~~didemnin~~ tamandarin ~~analog~~ has the following structure, wherein FL is a fluorophore



11. (Currently Amended) The ~~composition~~ compound of claim 1, wherein X is -NH-.

12. (Currently Amended) ~~The~~ A composition comprising the compound of claim 1 [[, further comprising]] and a pharmaceutically acceptable carrier.

13. (Currently Amended) A support having the tamandarin ~~analog~~ compound of claim 1 covalently attached thereto.

14. (Currently Amended) A method of inhibiting protein synthesis in a cell, the method comprising administering the ~~composition~~ compound of claim 1 to the cell.

15. (Currently Amended) A method of inhibiting growth of a cell, the method comprising administering the ~~composition~~ compound of claim 1 to the cell.

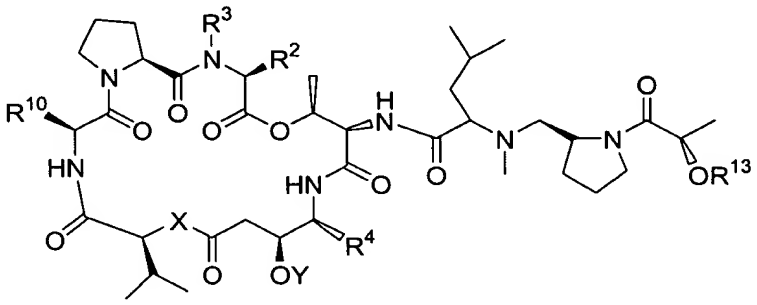
16. (Currently Amended) A method of inhibiting proliferation of a cell, the method comprising administering the ~~composition~~ compound of claim 1 to the cell.

17. (Currently Amended) A method of inhibiting tumorigenesis in a cell, the method comprising administering the ~~composition~~ compound of claim 1 to the cell.

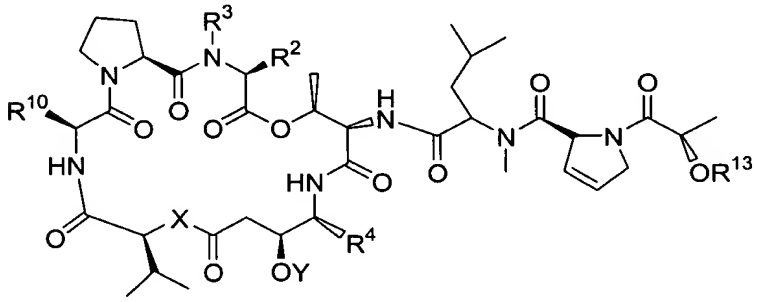
18. (Currently Amended) A method of enhancing apoptosis of a cell, the method comprising administering the ~~composition~~ compound of claim 1 to the cell.

19. (Currently Amended) A ~~composition comprising a~~ compound having a structure selected from the group consisting of

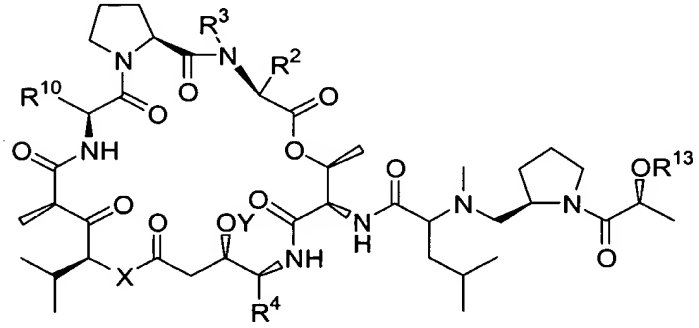
(a)



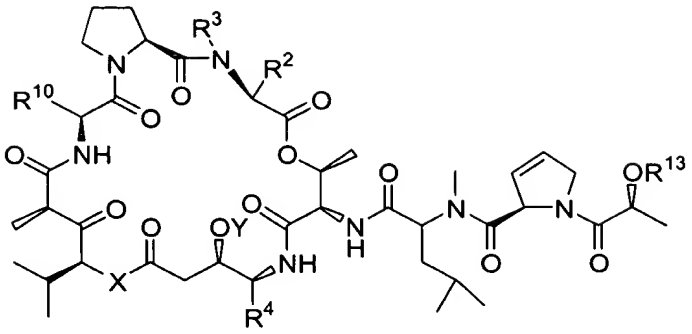
(b)



(c)



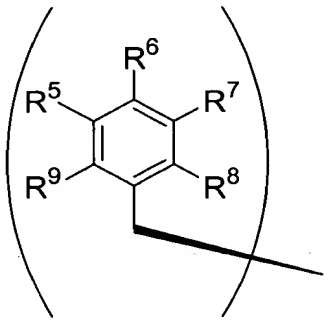
, and

(d) 

wherein:

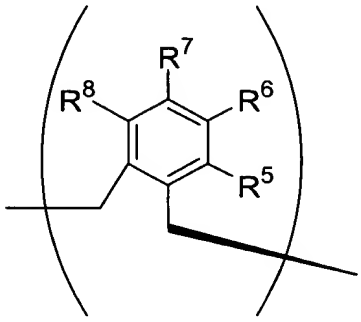
i) R^2 and R^3 are one of

(a) R^3 is selected from the group consisting of $-CH_3$ and -H; and R^2 is selected from the group consisting of an isoleucine side chain, a valine side chain, an alanine side chain, a norleucine side chain, a norvaline side chain, a proline side chain, a leucine side chain, a histidine side chain, a tryptophan side chain, an arginine side chain, a lysine side chain, a second fluorophore, and a substituent having the structure



; and

(b) R^2 and R^3 together are a substituent having the structure



;

ii) each of R^5, R^6, R^7, R^8, and R^9, when present, is independently selected from the group consisting of -H, -OH, $-OCH_3$, $-CO(C_6H_5)$, -Br, -I, -F, -Cl, $-CH_3$, and $-C_2H_5$;

iii) R^4 is selected from the group consisting of an isoleucine side chain and a valine side chain;

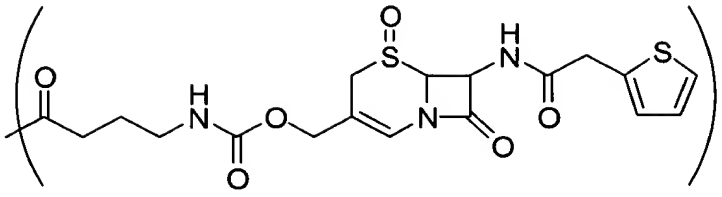
iv) X is selected from the group consisting of -O- and -NH-;

v) Y is selected from the group consisting of -H and a hydroxyl protecting group;

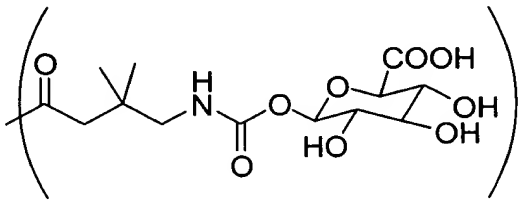
vi) R^{10} is selected from the group consisting of a leucine side chain and a lysine side chain; and

vii) R^{13} is an enzyme-cleavable moiety that is cleavable by an enzyme selected from the group consisting of a carboxypeptidase, a beta-lactamase, a beta galactosidase, a penicillin V-amidase, a cytosine deaminase, a nitroreductase, an alkaline phosphatase, a beta-glucuronidase, and a catalytic antibody.

20. (Currently Amended) The ~~composition~~ compound of claim 19, wherein R^{13} has the structure



21. (Currently Amended) The ~~composition~~ compound of claim 19, wherein R^{13} has the structure



22. (Currently Amended) A method of inhibiting protein synthesis in a cell, the method comprising administering the ~~composition~~ compound of claim 19 to the cell.

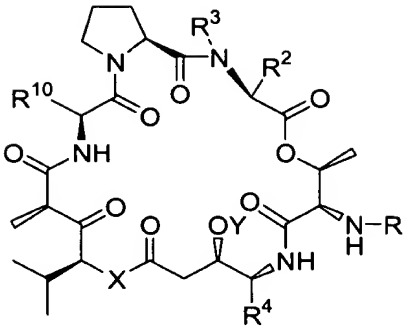
23. (Currently Amended) A method of inhibiting growth of a cell, the method comprising administering the ~~composition~~ compound of claim 19 to the cell.

24. (Currently Amended) A method of inhibiting proliferation of a cell, the method comprising administering the ~~composition~~ compound of claim 19 to the cell.

25. (Currently Amended) A method of inhibiting tumorigenesis in a cell, the method comprising administering the ~~composition~~ compound of claim 19 to the cell.

26. (Currently Amended) A method of enhancing apoptosis of a cell, the method comprising administering the ~~composition~~ compound of claim 19 to the cell.

27. (Currently Amended) A ~~composition comprising a~~ didemnin compound ~~analog~~ having the structure



wherein:

i) R^1 is selected from the group consisting of

-(N-methyl)leucine-deoxo-proline,

-(N-methyl)leucine-deoxo-proline-lactate,

-(N-methyl)leucine-deoxo-proline-pyruvate,

-(N-methyl)leucine-deoxo-proline-lactate-(a first fluorophore),

-(N-methyl)leucine-deoxo-proline-lactate-glutamine-pyroglutamate,

-(N-methyl)leucine-deoxo-proline-lactate-glutamine-cyclopentanoate,

-(N-methyl)leucine-deoxo-proline-alanine-leucine-pyroglutamate,

-(N-methyl)leucine-deoxo-proline-(N-methyl-alanine)-leucine-pyroglutamate,

-(N-methyl)leucine-dehydro-proline,

-(N-methyl)leucine-dehydro-proline-lactate,

-(N -methyl)leucine-dehydro-proline-pyruvate,

-(N-methyl)leucine-dehydro-proline-lactate-(a first fluorophore),

-(N-methyl)leucine-dehydro-proline-lactate-glutamine-pyroglutamate,

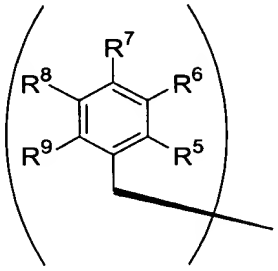
-(N-methyl)leucine-dehydro-proline-lactate-glutamine-cyclopentanoate,

-(N-methyl)leucine-dehydro-proline-alanine-leucine-pyroglutamate, and

-(N-methyl)leucine-dehydro-proline-(N-methyl-alanine)-leucine-pyroglutamate;

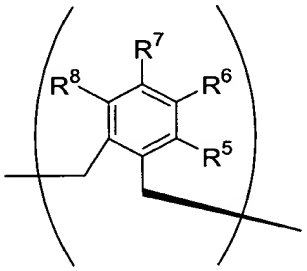
ii) R^2 and R^3 are one of

(a) R^3 is selected from the group consisting of $-CH_3$ and -H; and R^2 is selected from the group consisting of an isoleucine side chain, a valine side chain, an alanine side chain, a norleucine side chain, a norvaline side chain, a leucine side chain, a histidine side chain, a tryptophan side chain, an arginine side chain, a lysine side chain, a second fluorophore, and a substituent having the structure



; and

(b) R^2 and R^3 together are a substituent having the structure



;

iii) each of R^5, R^6, R^7, R^8, and R^9, when present, is independently selected from the group consisting of -H, -OH, $-OCH_3$, $-CO(C_6H_5)$, -Br, -I, -F, -Cl, $-CH_3$, and $-C_2H_5$;

iv) R^4 is selected from the group consisting of an isoleucine side chain and a valine side chain;

v) X is selected from the group consisting of -O- and -NH-;

vi) Y is selected from the group consisting of -H and a hydroxyl protecting group; and

vii) R^{10} is selected from the group consisting of a leucine side chain and a lysine side chain [[; and

viii) the molecule is not tamandarin A]].

28. (Currently Amended) The ~~composition~~ compound of claim 27, wherein R^1 is selected from the group consisting of

-(N-methyl)leucine-deoxo-(S)proline,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate,

-(N-methyl)leucine-deoxo-(S)proline-pyruvate,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(a first fluorophore),

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-glutamine-pyroglutamate,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-glutamine-cyclopentanoate,

-(N-methyl)leucine-deoxo-(S)proline-alanine-leucine-pyroglutamate,

-(N-methyl)leucine-deoxo-(S)proline-(N-methyl-alanine)-leucine-pyroglutamate,

-(N-methyl)leucine-dehydro-(S)proline,

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate,

-(N-methyl)leucine-dehydro-(S)proline-pyruvate,

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate-(a first fluorophore),

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate-glutamine-pyroglutamate,

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate-glutamine-cyclopentanoate,

-(N-methyl)leucine-dehydro-(S)proline-alanine-leucine-pyroglutamate and

-(N-methyl)leucine-dehydro-(S)proline-(N-methyl-alanine)-leucine-pyroglutamate.

29. (Currently Amended) The ~~composition~~ compound of claim 27, wherein R^1 is selected from the group consisting of

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(S)glutamine-(S)pyroglutamate,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(S)glutamine-(S)cyclopentanoate,

-(N-methyl)leucine-deoxo-(S)proline-(S)alanine-(S)leucine-(S)pyroglutamate,

-(N-methyl)leucine-deoxo-(S)proline-(N-methyl-S-alanine)-(S)leucine-(S)pyroglutamate,

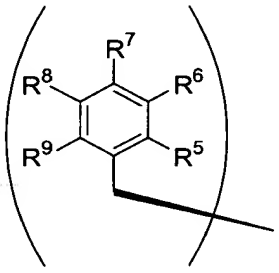
-(N-methyl)leucine-dehydro-(S)proline-(S)lactate-(S)glutamine-(S)pyroglutamate,

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate-(S)glutamine-(S)cyclopentanoate,

-(N-methyl)leucine-dehydro-(S)proline-(S)alanine-(S)leucine-(S)pyroglutamate, and

-(N-methyl)leucine-dehydro-(S)proline-(N-methyl-S-alanine)-(S)leucine-(S)pyroglutamate.

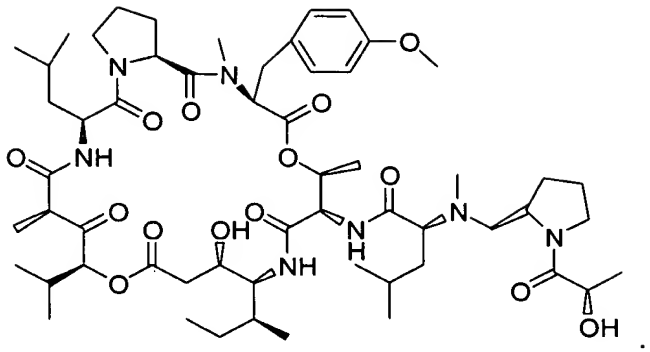
30. (Currently Amended) The ~~composition~~ compound of claim 27, wherein R^2 is



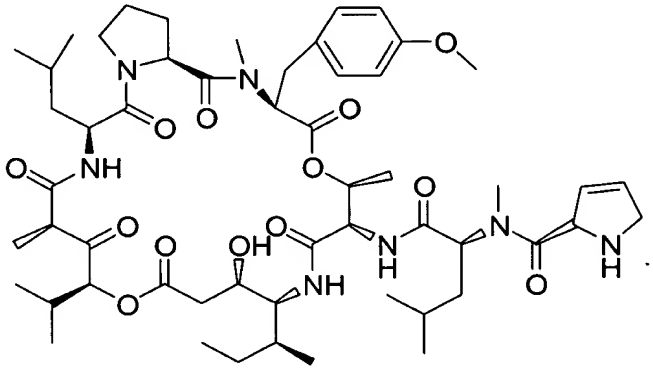
,

R^3 is methyl, R^4 is an isoleucine side chain, each of R^5, R^6, R^8, and R^9 is -H, R^7 is methoxy, R^{10} is a leucine side chain, X is -O-, and Y is -H.

31. (Currently Amended) The compound of claim 27, wherein the didemnin ~~analog~~ is compound 202 having the structure

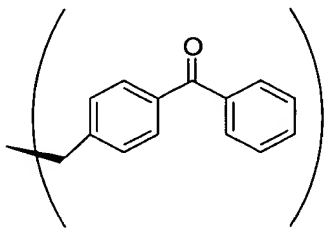


32. (Currently Amended) The ~~composition~~ compound of claim 27, wherein the didemnin ~~analog~~ is compound 204 having the structure



33. (Currently Amended) The ~~composition~~ compound of claim 27, wherein R^1 is -(N-methyl)leucine-deoxo-(S)proline-lactate.

34. (Currently Amended) The ~~composition~~ compound of claim 27, wherein Y is -H, and wherein R^2 has the structure



35. (Currently Amended) The ~~composition~~ compound of claim 27, wherein R^2 is a lysine side chain and Y is -H.

36. (Currently Amended) The ~~composition~~ compound of claim 27, wherein X is -NH-.

37. (Currently Amended) ~~The~~ A composition comprising the compound of claim 27 [[, further comprising]] and a pharmaceutically acceptable carrier.

38. (Currently Amended) A support covalently attached with the didemnin analog of claim 27.

39. (Currently Amended) A method of inhibiting protein synthesis in a cell, the method comprising administering the ~~composition~~ compound of claim 27 to the cell.

40. (Currently Amended) A method of inhibiting growth of a cell, the method comprising administering the ~~composition~~ compound of claim 27 to the cell.

41. (Currently Amended) A method of inhibiting proliferation of a cell, the method comprising administering the ~~composition~~ compound of claim 27 to the cell.

42. (Currently Amended) A method of inhibiting tumorigenesis in a cell, the method comprising administering the ~~composition~~ compound of claim 27 to the cell.

43. (Currently Amended) A method of enhancing apoptosis of a cell, the method comprising administering the ~~composition~~ compound of claim 27 to the cell.

44. (Previously Presented) A method of preparing a tamandarin or didemnin analog comprising incorporating a deoxo-proline residue in place of a proline residue of the analog in a chemical reaction to prepare said tamandarin or didemnin analog.

45. (Previously Presented) The method of claim 44, wherein the analog comprises an (N-methyl)leucine-proline moiety and wherein the (N-methyl)leucine-proline moiety is replaced by an (N-methyl)leucine-deoxo-proline moiety.

46. (Previously Presented) The method of claim 45 wherein the (N-methyl)leucine-deoxo-proline is made by

reducing the ester function of proline to an aldehyde function; and

coupling the proline with the (N-methyl)leucine moiety by reductive amination to yield the (N-methyl)leucine-deoxo-proline moiety.

47. (Previously Presented) The method of claim 46, wherein the amine moiety of the proline is protected with an amine-protecting group prior to the reductive amination.

48. (Previously Presented) The method of claim 46, wherein the ester function of the proline is reduced to an aldehyde function by contacting the proline with a strong base and then contacting the proline with an oxidizing agent.

49. (Previously Presented) The method of claim 46, wherein the reductive amination is performed in a non-aqueous solvent in the presence of a strong base and a carboxylic acid catalyst.

50. (Previously Presented). A method of preparing a tamandarin or didemnin analog the improvement comprising incorporating a dehydro-proline residue in place of a proline residue of the analog in a chemical reaction used to prepare said tamandarin or didemnin analog.

51. (Previously Presented) The method of claim 50, wherein the analog comprises an (N-methyl)leucine-proline moiety and wherein the (N-methyl)leucine-proline moiety is replaced by an (N-methyl)leucine-dehydro-proline moiety.

52. (Previously Presented) The method of claim 50, wherein the dehydro-proline residue is made by protecting the carboxyl and amino moieties of the 4-hydroxyprolinate, alkyl sulfonylating the 4-hydroxyl moiety, displacing the alkyl-sulfonate moiety with an aryl-selenyl moiety, oxidatively eliminating the aryl-selenyl moiety to yield a dehydro-proline moiety having protected carboxyl and amine moieties, and coupling the dehydro-proline moiety with an amine moiety of the analog.

53. (Previously Presented) The method of claim 50, wherein the alkyl-sulfonate moiety is a methyl-sulfonate moiety.

54. (Previously Presented) The method of claim 50, wherein the aryl-selenyl moiety is a phenyl-selenyl moiety.

55. (Previously Presented) The method of claim 50, wherein the 4-hydroxyprolinate is trans-4-hydroxyprolinate.

56. (Currently Amended) The ~~composition~~ compound of claim 1, wherein the ~~analog~~ compound is substantially pure.

57. (Currently Amended) The ~~composition~~ compound of claim 5, wherein the ~~analog~~ compound is substantially pure.

58. (Currently Amended) The ~~composition~~ compound of claim 6, wherein the ~~analog~~ compound is substantially pure.

59. (Currently Amended) The ~~composition~~ compound of claim 10, wherein the ~~analog~~ compound is substantially pure.

60. (Currently Amended) The ~~composition~~ compound of claim 19, wherein the ~~analog~~ compound is substantially pure.

61. (Currently Amended) The ~~composition~~ compound of claim 27, wherein the ~~analog~~ compound is substantially pure.

62. (New) A composition comprising the compound of claim 19 and a pharmaceutically acceptable carrier.